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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,880	07/10/2003	Benjamin David Silverman	YOR920030162US1	2640

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EXAMINER
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NEGIN, RUSSELL SCOTT

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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<b>Office Action Summary</b>	<b>Application No.</b> 10/616,880	<b>Applicant(s)</b> SILVERMAN, BENJAMIN DAVID	
	<b>Examiner</b> Russell S. Negin	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 27 July 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 10-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 14-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____   | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-9 and 14-21 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Upon further consideration of the recent Official Gazette notice of November 22, 2005, entitled, "Interim Guidelines for examination of patent applications for patent subject matter eligibility," ([www.uspto.gov/web/offices/com/sol/og/2005/week47/patgupa.htm](http://www.uspto.gov/web/offices/com/sol/og/2005/week47/patgupa.htm)), it is the decision of the Office to enact a 35 U.S.C. 101 rejection.

In regards to claims 1-9 and 14-21, the instant claims are drawn to a biophysical algorithm. A biophysical algorithm is non-statutory unless the claims include a step of physical transformation, or if the claims include a useful, tangible and concrete result. It is important to note, that the claims themselves must include a physical transformation step or a useful, tangible and concrete result in order for the claimed invention to be statutory. It is not sufficient that a physical transformation step or a useful, tangible, and concrete result be asserted in the specification for the claims to be statutory. In the instant claims, there is no step of physical transformation, thus the Examiner must determine if the instant claims include a useful, tangible, and concrete result.

In determining if the instant claims are useful, tangible, and concrete, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, substantial, and credible. For a claim to be "tangible," the claim must set forth a practical application of the invention that produces a real-world result. For a claim to be "concrete," the process must have a result that can be substantially repeatable or the process must substantially produce the same result again. Furthermore, the claim must recite a useful, tangible, and concrete result in the claim itself, and the claim must be limited only to statutory embodiments. Thus, if the claim is broader than the statutory embodiments of the claim, the Examiner must reject the claim as non-statutory.

Claims 1-9 and 14-21 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the method is outputted to a display or a memory or another computer on a network, or by including a physical transformation.

As stated in the Official Gazette notice, "The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing. However, the tangible requirement does require that the claim must recite more than a Sec. 101 judicial exception, in that the process claim must set forth a practical application of that Sec. 101 judicial exception to produce a real-world result. Benson, 409 U.S. at 71-72, 175 USPQ at 676-77 (invention ineligible because had "no substantial practical

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application."). "[A]n application of a law of nature or mathematical formula to a . . . process may well be deserving of patent protection." Diehr, 450 U.S. at 187, 209 USPQ at 8 (emphasis added); see also Corning, 56 U.S. (15 How.) at 268, 14 L.Ed. 683 ("It is for the discovery or invention of some practical method or means of producing a beneficial result or effect, that a patent is granted . . ."). In other words, the opposite meaning of "tangible" is "abstract.""

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Silverman [PNAS; April 24, 2001; volume 98, pages 4996-5001].

Claims 1-9 state:

1. A method for calculating a moment of a tertiary protein structure comprising a plurality of residues, the method comprising the steps of:
  - calculating a centroid of residue centroids; using the centroid of residue centroids as a spatial origin of a global linear hydrophobic moment;
  - enhancing correlation between residue centroid magnitude and residue solvent accessibility; and
  - defining the global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global linear hydrophobic moment.
2. The method of claim 1, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric.

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3. The method of claim 1, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using an ellipsoidal metric.
4. The method of claim 1, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a solvent accessibility metric.
5. The method of claim 1, wherein the centroid of residue centroids represents a geometric center of the tertiary protein structure.
6. The method of claim 1, wherein the global linear hydrophobic moment characterizes an amphiphilicity of the tertiary protein structure.
7. The method of claim 1, wherein the global linear hydrophobic moment characterizes a magnitude of amphiphilicity of the tertiary protein structure.
8. The method of claim 1, wherein the global linear hydrophobic moment characterizes a direction of amphiphilicity of the tertiary protein structure.
9. The method of claim 1, wherein the global linear hydrophobic moment is used to identify functional regions of the tertiary protein structure.

The article of Silverman, "Hydrophobic moments of protein structures: Spatially profiling the distribution," describes how to calculate moments of tertiary protein structures.

In equation [12] on page 4997 of Silverman,  $r_i$  is the vector pointing to the centroid of residue  $i$  while  $r_c$  is the vector pointing to the centroid of the entire protein molecule (i.e. the geometric center of the protein).

In equation [13] on page 4998 of Silverman, a first order hydrophobic moment imbalance about the entire protein is written, accounting for hydrophobicity and solvent accessible surface area. Each centroid of every protein residue contributes to this global moment.

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In equations [13] and [14] on page 4998 of Silverman, distance metrics, ellipsoidal metrics, and a solvent accessibility are all used to enhance the centroid magnitude.

The global linear hydrophobic moment characterizes the amphiphilicity, and the magnitude and direction of the amphiphilicity of the tertiary protein structure.

Figure 6 on page 5000 of Silverman shows how an arm of the protein can be identified as it falls outside the ellipse characterizing the hydrophobic moment of the protein.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 14-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Silverman [PNAS; April 24, 2001; volume 98, pages 4996-5001] in view of Michaud [USPAT 4,017,721].

14. An apparatus for calculating a moment of a tertiary protein structure comprising a plurality of residues, the apparatus comprising: a memory; and at least one processor operative to: calculate a centroid of residue centroids; use the centroid of residue centroids as a spatial origin of a global linear hydrophobic moment; enhance correlation between residue centroid magnitude and residue solvent accessibility; and define the global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global linear hydrophobic moment.

15. The apparatus of claim 14, wherein the centroid of the residue centroids represents

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a geometric center of the tertiary protein structure.

16. The apparatus of claim 14, wherein the global linear hydrophobic moment characterizes an amphiphilicity of the tertiary protein structure.

17. The apparatus of claim 14, wherein the global linear hydrophobic moment is used to identify functional regions of the tertiary protein structure.

18. The apparatus of claim 14, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric.

19. The apparatus of claim 14, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using an ellipsoidal metric.

20. The apparatus of claim 14, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a solvent accessibility metric.

21. An article of manufacture for calculating a moment of a tertiary protein structure comprising a plurality of residues, comprising: a computer-readable medium having computer-readable code embodied thereon, the computer-readable code comprising: a step to calculate a centroid of residue centroids; a step to use the centroid of residue centroids as a spatial origin of a global linear hydrophobic moment; a step to enhance correlation between residue centroid magnitude and residue solvent accessibility; and a step to define the global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global linear hydrophobic moment.

The article of Silverman, "Hydrophobic moments of protein structures: Spatially profiling the distribution," describes how to calculate moments of tertiary protein structures.

In equation [12] on page 4997 of Silverman,  $r_i$  is the vector pointing to the centroid of residue  $i$  while  $r_c$  is the vector pointing to the centroid of the entire protein molecule (i.e. the geometric center of the protein).

In equation [13] on page 4998 of Silverman, a first order hydrophobic moment imbalance about the entire protein is written, accounting for hydrophobicity and solvent



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accessible surface area. Each centroid of every protein residue contributes to this global moment.

In equations [13] and [14] on page 4998 of Silverman, distance metrics, ellipsoidal metrics, and a solvent accessibility are all used to enhance the centroid magnitude.

The global linear hydrophobic moment characterizes the amphiphilicity, and the magnitude and direction of the amphiphilicity of the tertiary protein structure.

However, the article of Silverman does not teach a computer apparatus of programmable media for performing the claimed analysis.

The patent of Michaud, entitled, "Method and apparatus for determining the position of a body," uses a digital analysis system to calculate a centroid of a body. It is inherent, that in this computer system, there is some sort of computer programmable media to control the computer system.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice Silverman in view of Michaud because Michaud has the advantage of using a computerized system to calculate centroids of objects which could potentially be used in Silverman to duplicate the instant invention.

### ***Response to Arguments***

Applicant's arguments filed 27 July 2006 have been fully considered but they are not persuasive.

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Applicant has two main arguments against the 35 U.S.C. 102(b) rejection. The first is stated on page 2 of the "Remarks," "the Silverman reference does not teach or suggest the step of enhancing correlation between residue centroid magnitude and residue solvent accessibility within the context of a global linear hydrophobic moment." The second argument of the applicant is on page 3 of the "Remarks" that Silverman is mainly devoted to teaching zero and second order moments and not first order moments as claimed in the present invention.

To address these arguments, the last four lines in the second column of page 4997 of Silverman to the first five lines on page 4998 of Silverman state, "The first-order moment calculated about the centroid of the protein is, therefore, a measure of first order hydrophobic imbalance about the mean. With the inclusion of values of the solvent-accessible surface area,  $s_i$ , for each of the residues, the surface exposed first-order hydrophobic moment imbalance about the entire protein can be then written [eq 13 is given]. This moment could provide useful information with respect to the three dimensional spatial affinity of the tertiary protein structure and external structures with which it might interact."

Consequently, the first-order moment is discussed in detail as about "the entire protein," and is interpreted as the global first-order moment. Additionally, even if the reference did not talk about the "correlation between residue centroid magnitude and residue solvent accessibility within the context of a global linear hydrophobic moment," the relevant second method step of claim 1 does not state that this enhanced correlation has to be within the context of a global linear moment.

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Applicant argues on page 4 of the "Remarks" that the obviousness prior art rejection is inappropriate because the secondary (Michaud) reference does not make up for the deficiencies in the Silverman reference. Since the Silverman reference does not have the claimed deficiencies, the obviousness prior art reject is still valid.

### **Conclusion**

No claim is allowed

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Andrew Wang, Supervisory Patent Examiner, can be reached at (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Yolanda Chadwick, whose telephone number is (571) 272-0514.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RSN  
6 October 2006

*RSN*  
6 October 2006

*John S. Brusca 10 October 2006*  
**JOHN S. BRUSCA, PH.D**  
**PRIMARY EXAMINER**